

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

AN 1962:53395 CAPLUS Full-text

DN 56:53395

OREF 56:10137d-i,10138a-g

TI Phenoxazines. II. 10-Dialkylaminoalkylphenoxazines

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CS Univ. Louvain, Belg.

SO Journal of Organic Chemistry (1961), 26, 3827-31

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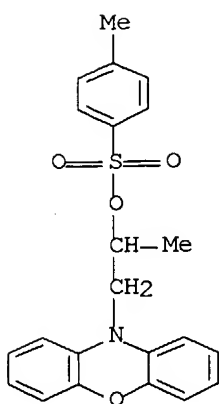
DT Journal

LA Unavailable

AB cf. CA 55, 1621e. The preparation of a number of 10-dialkylaminoalkyl derivs. of phenoxazine (I) and of 2-ethylphenoxazine (H) was described. Various methods of synthesis were examined Method A. I (51.6 g.), 12.4 g. NaNH₂, and 150 ml. PhMe refluxed 1 hr., 42.1 g. 3-pyrrolidinopropyl chloride in 50 ml. PhMe added dropwise, the mixture refluxed 2 hrs., treated with H₂O, extracted with dilute HCl, the acid exts. made alkaline, extracted with C₆H₆, and evaporated gave 3 g. unchanged I. The C₆H₆ extract afforded 62 g. 10-(3-pyrrolidinopropyl)phenoxazine (III), b₃ 220-2°; HCl salt m. 162-3°. Method B. I (7.32 g.) added to NaNH₂ (prepared by dissolving 1.01 g. Na in 40 ml. NH₃ containing a crystal of Fe(NO₃)₃), stirred 0.25 hr., 6.3 g. 1-chloro-3-bromopropane added, after 0.5 hr. the NH₃ evaporated, H₂O added, extracted with Et₂O, dried, and evaporated gave a residue. The residue in 25 ml. PhMe, 5.68 g. pyrrolidine, and a small amount of Cu powder heated 48 hrs. at 100-10° gave 7.61 g. III. The residue after evaporation of the Et₂O upon distillation gave 77% 10-(3-chloropropyl)phenoxazine, m. 54-5° (alc.). I (29.2 g.) and 6.4 g. NaNH₂ in 80 ml. PhMe refluxed 1 hr., stirred 3 hrs. with 10 g. propylene oxide, left overnight, filtered, the solution treated with H₂O, evaporated, extracted with C₆H₆, dried, and evaporated gave 30.4 g. 10-(2-hydroxypropyl)phenoxazine (IV), m. 95-8°. When propylene chlorohydrin was used, the only product was unchanged I. (8.4 g.) with 3.5 g. propylene oxide gave 5.35 g. 2-ethyl-10-(2-hydroxypropyl)phenoxazine, m. 78-80°, b_{0.4} 190°. p-MeC₆H₄SO₂Cl (25 g.) in 30 ml. C₅H₅N added to 29.5 g. IV in 40 ml. C₅H₅N, the mixture stirred 2 hrs., left overnight, treated with ice H₂O, the solid filtered off, and the product recrystd. gave 40 g. 10-[2-(p-tolylsulfonyloxy)propyl]phenoxazine (V), m. 136-8° (alc.-Me₂CO). 2-Ethyl-10-[2-(p-tolylsulfonyloxy)propyl]phenoxazine was similarly prepared, m. 85-6° (alc.). Method C. V (3 g.) added to 3 g. NHEt₂ in 30 ml. PrOH, the mixture heated 48 hrs. at 120° in a closed vessel, evaporated, the residue dissolved in 10% NaOH, the organic base extracted with dilute HCl, made alkaline, extracted with Et₂O, and evaporated gave 0.3 g. 10-(2-diethylaminopropyl)phenoxazine-HCl (VI), m. 208-10° (alc.). I (7.32 g.) treated with 1-diethylamino-2-chloropropane in the presence of NaNH₂ gave 7.1 g. base, distilled at 180°/1 mm. The base neutralized with HCl in alc. gave 5.43 g. HCl salt and 2.14 g. 2nd crop. The first product dissolved in H₂O, extracted with Et₂O after being made alkaline, and treated with picric acid gave 4.78 g. picrate, m. 152-3° (decomposition). The picrate was turned into VI by extraction with Et₂O, made basic, evaporated, and neutralized with HCl. The 2nd product was purified through the picrate, m. 152-3°, to give the HCl salt of 10-(2-diethylaminoisopropyl)phenoxazine, m. 162-4°. I (11 g.) and 2.8 g. NaNH₂ in 30 ml. PhMe refluxed 1 hr., treated 4 hrs. at room temperature with 10.9 g. Et β-bromopropionate, refluxed 0.5 hr., treated with H₂O, extracted with C₆H₆, the extract, dried, and evaporated gave

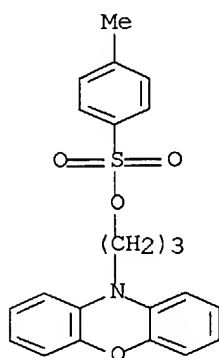
7.3 g. Et β -(10-phenoxazinyl)propionate (VII), b₂ 210°. VII (7.3 g.) in 40 ml. Et₂O added to 1.4 g. LiAlH₄ in 60 ml. Et₂O, the mixture refluxed 2 hrs., cooled, decomposed, made acidic, extracted with Et₂O, and the residue distilled gave 4.54 g. 10-(3-hydroxypropyl)phenoxazine (VIII), m. 68°. VIII treated with p-MeC₆H₄SO₂Cl in C₅H₅N gave 10-[3-(p-tolylsulfonyloxy)propyl]phenoxazine, m. 52-4°, resolidified, and m. 158°. II (12.6 g.) and 2.5 g. NaNH₂ in 60 ml. xylene refluxed 1 hr., 10.8 g. 2-(3-chloropropoxy)tetrahydropyran in 20 ml. xylene added, the mixture refluxed 48 hrs., cooled, treated with H₂O, extracted with Et₂O, and distilled. At 160° 2.5 g. unchanged II was recovered and at 230° 12 g. tetrahydropyranyloxypropyl derivative (IX). IX taken up in 80 ml. 75% alc. and 1.5 ml. concentrated HCl, refluxed 1 hr., distilled, the residue extracted with Et₂O, and distilled gave 7.2 g. 2-ethyl-10-(3-hydroxypropyl)-phenoxazine (X), b_{0.5} 230°. PBr₃ (20 g.) added to 12 g. X in 20 ml. CHCl₃, the mixture refluxed 1 hr. on the steam bath, washed, and the CHCl₃ solution evaporated gave 1.3 g. 2-ethyl-10(3-bromopropyl)phenoxazine. The following 10-dialkyl-aminoalkyl derivs. of I were thus obtained in addition to the ones described above (10-side chain, method, b.p. of base/mm., % yield, and m.p. of salt and salt given): CH₂CH₂, NMe₂, A, 145-50°/1, 51, 237-8°, HCl; CH₂CH₂NEt₂, A, 160-70°/1, 57, 167-9°, HCl; 2-piperidinoethyl, A, 170°/0.3, 44, 203-5° HCl; 2-morpholinoethyl, A, 170°/1, 30, 226-7°, HCl; CH₂CHMeNMe₂, A, 160-70°/1, 70, 175-7°, HCl; 2-(4-methylpiperazino)-ethyl, A, 185°/1, 50, 258-60°, 2HCl; 2-piperidinopropyl, C, 200°/0.7, 24, 98-200°, HCl; CH₂CH₂CH₂NMe₂, A, 190°/0.5, 58, 132-4°, HCl; CH₂CH₂CH₂NEt₂, A, -, 70, 112-14°, succinate; CH₂CH₂NPr₂, B, 210°/1, 64, 152-3°, HCl; 3-morpholinopropyl, B, 230°/1, 65, 195-6°, HCl; 3-piperidinopropyl, B, -, 76, 197-9°, HCl; 3-piperidinopropyl, C, -, 30, -; 3-(4-methylpiperazino)-propyl, A, 190°/1, 66, 245-6°, 2HCl; 3-[4-(2-hydroxyethyl)piperazino]propyl, B, 250°/1, 53, 236-7°, 2HCl; CH₂CHMeCH₂NMe₂, A, 170°/1, 64, 161-3°, HCl; CH₂CHMeCH₂NEt₂, A, 190°/0.5, 60, 156-8°, HCl; 2-methyl-3-piperidinopropyl, A, 200°/0.8, 56, 170-1°, HCl. The following 10-dialkylaminoalkylderivs. of II were similarly obtained (side chain, method, b.p./mm. of base, % yield, and m.p. of the salt, and salt given): CH₂CH₂NEt₂, A, 210°/1, 69, 158-60°, HCl; 2-(4-methyl piperazino)ethyl, A, 210°/0.5, 65, 267-9°, 2HCl; CH₂CHMeNEt₂, C, 180°/0.3, 17, 178-80°, HCl; 2-piperidino-propyl, C, 200°/0.5, 20, 201-3°, HCl; CH₂CH₂CH₂NMe₂, A, 200°/1, 64, 208-9°, HCl; CH₂CH₂CH₂NEt₂, A, 210°/0.1, 50, 119-21°, succinate; CH₂CH₂NEt₂, B, 200°/0.6, 33, -, -; 3-piperidinopropyl, A, 230°/1, 92, 174-5°, HCl; 3-piperidinopropyl, B, 210°/0.7, 40, -, -; 3-piperidinopropyl, D, -, 33, -, -; 3-(4-methylpiperazino)propyl, A, 230°/1, 68, 256-7°, 2HCl; 3-[4-(2-hydroxyethyl)piperazino]propyl, D, 250°/0.2, 26, 238-40°, 2HCl; CH₂CHMeCH₂NMe₂, A, 185°/0.7, 68, 144-6°, fumarate; CH₂CHMeCH₂NEt₂, A, 190°/0.3, 74, 126-9°, fumarate; 2-methyl-3-piperidinopropyl, A, 190°/0.3, 73, 171-3°, HCl; 2-methyl-3-(4-methylpiperazino)propyl, A, 210°/0.3, 78, 215-17°, 2HCl.

- IT 95137-74-9, Phenoxazine-10-ethanol, α -methyl-,
p-toluenesulfonate 95137-75-0, Phenoxazine-10-propanol,
p-toluenesulfonate 95623-30-6, Phenoxazine-10-ethanol,
2-ethyl- α -methyl-, p-toluenesulfonate
(preparation of)
RN 95137-74-9 CAPLUS
CN Phenoxazine-10-ethanol, α -methyl-, p-toluenesulfonate (6CI, 7CI)
(CA INDEX NAME)



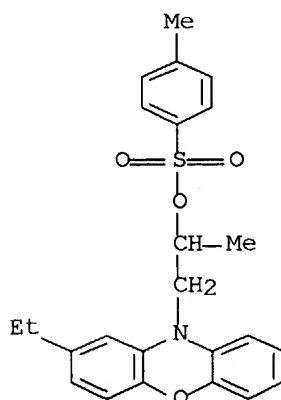
RN 95137-75-0 CAPLUS

CN Phenoxazine-10-propanol, p-toluenesulfonate (6CI, 7CI) (CA INDEX NAME)



RN 95623-30-6 CAPLUS

CN Phenoxazine-10-ethanol, 2-ethyl- α -methyl-, p-toluenesulfonate (6CI, 7CI) (CA INDEX NAME)



L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1960:28856 CAPLUS Full-text
 DN 54:28856
 OREF 54:5708f-i,5709a-i,5710a-d
 TI Phenoxazine derivatives
 PA Recherche et industrie therapeutiques (R.I.T.) S.A.
 DT Patent
 LA Unavailable

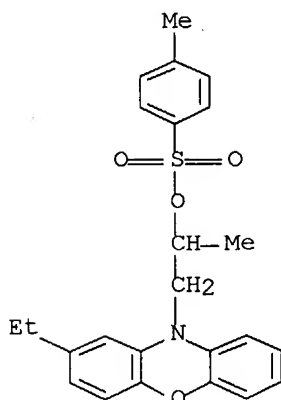
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	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	BE 575133		19590727	BE	
AB.	<p>3-Acetylphenoxazine (I) is prepared as follows. 10-Acetylphenoxazine (22.5 g.) in 400 cc. CS₂ is slowly added with stirring to 40 g. anhydrous AlCl₃, the mixture refluxed hr., 11.7 g. AcCl added maintaining ebullition, the mixture refluxed 2 hrs., then cooled, decanted, ice and 10 cc. HCl added, the precipitate washed with H₂O, refluxed with 200 cc. AcOH and 50 cc. HCl 10 min., after cooling the precipitate washed with H₂O and dried, extracted with C₆H₆, and crystallized to afford 20.2 g. yellowish green product, m. 211-13°. 3-Propionylphenoxazine, m. 216-18°, 3-butyrylphenoxazine, m. 107-8°, and 3-chloroacetylphenoxazine, m. 218-19°, are similarly prepared 3-Ethylphenoxazine (II) is prepared by refluxing 15 min. 150 cc. ethylene glycol, 28 g. I, and 21 cc. 78% aqueous N₂H₄.H₂O, 21 g. KOH in 75 cc. hot ethylene glycol added, the mixture refluxed 1 hr. before dehydration at 195°, after 3 hrs. reflux cooled at 100°, 500 cc. EtOH and 750 cc. H₂O added, the precipitate washed with H₂O, dried at 60° under vacuum, and distilled to afford 21 g. II, b0.7 170°, m. 110-12°. 3-Acetylphenoxazine-10-carboxylic acid chloride is prepared by adding 17 cc. 30% COCl₂-toluene to 5.5 g. I in 12 cc. toluene and heating at 125° during 3 hrs. After cooling and evaporating to dryness, the residue is dissolved in C₆H₆, treated with active C, and crystallized to yield 6 g. product, m. 149-51°. 3-Ethyl-10-(β-diethylaminoethyl)phenoxazine is prepared by refluxing 45 min. a stirred mixture of 4.2 g. II, 0.78 g. NaNH₂, and 15 cc. anhydrous toluene and adding 3.4 g. α-chloro-β-diethylaminoethane-HCl in 6 cc. anhydrous toluene. After 2 hrs. refluxing then cooling, 30 cc. H₂O is added, the aqueous layer extracted with 3 cc. C₆H₆, and the joined organic solns. washed with H₂O and dried. Distillation yields 4.13 g. base, b1 210°; hydrochloride m. 158-60°. This procedure is applied to preparation of the following products: 3-ethyl-10-(γ-dimethyl-aminopropyl)phenoxazine, b1 200°, hydrochloride, m. 208-9°; 3-ethyl-10-[β-(N'-methylpiperazino)ethyl]phenoxazine, b0.6 210°, in 4.51-g. yield from 5.1 g. α-chloro-β-(N'-methylpiperazino)ethane, di-HCl salt, m. 267-9° (decomposition); 3-ethyl-10-[γ-(N'-methylpiperazino)propyl]phenoxazine, b1 230°, di-HCl salt, m. 256-7° (decomposition); 3-ethyl-10-(γ-dimethylamino-β-methylpropyl)phenoxazine, b1 190°, acid fumarate, m. 143-6°; 3-ethyl-10-(γ-diethylamino-β-methylpropyl)phenoxazine, b0.3 190°, acid fumarate, m. 126-9°; 3-ethyl-10-(γ-pyrrolidino-β-methylpropyl)phenoxazine, b0.25 190°, hydrochloride, m. 173°; 3-ethyl-10-[γ-(N'-methylpiperazino)-β-methylpropyl]phenoxazine, b0.25 210°, di-HCl salt, m. 215-7°; 3-ethyl-10-(γ-diethylaminopropyl)phenoxazine (IIa), b0.9 210°, acid succinate, m. 119-21°. IIa is also obtained by adding successively with stirring 4.2 g. II and 3.15 g. 1,2,3-trichloropropane to 0.505 g. Na in 20 cc. liquid NH₃ containing a crystal of Fe(NO₃)₃.</p>				

After NH₃ evaporation, the residue is treated with H₂O and Et₂O, the ether solution washed, dried, and evaporated, the residue mixed with 13 cc. toluene containing a small amount of powdered Cu and 2.92 g. Et₂NH, after heating at 100° 48 hrs. and cooling H₂O added, the aqueous layer extracted with Et₂O, the joined organic solns. washed, dried, and evaporated, and distilled to yield 2.07 g. base, b_{0.6} 200°. 3-Ethyl-10-(γ-pyrrolidinopropyl)phenoxazine, b_{0.7} 210°, is similarly obtained in 2.57-g. yield from 2.85 g. pyrrolidine to afford 1.9 g. corresponding hydrochloride (IIb), m. 174-5°. IIb is also obtained by heating at 100° 48 hrs. 4.5 g. 3-ethyl-10-(γ-bromopropyl)phenoxazine (III), 2.12 g. pyrrolidine, and powdered Cu in 10 cc. anhydrous toluene and converting the base into the corresponding hydrochloride in 1.6-g. yield. Similarly, 3-ethyl-10-{γ-[N'-(β-hydroxyethyl)piperazino]propyl}phenoxazine, b_{0.2} 260°, is obtained in 2.64-g. yield from 4.5 g. III and 3.9 g. N-(β-hydroxyethyl)piperazine to afford 0.62 g. di-HCl salt, m. 238-40°. II (12.6 g.) and 2.5 g. NaNH₂ in 60 cc. xylene is refluxed 1 hr. before addition of 10.8 g. 2-(3-chloropropoxy)tetrahydropyran in 20 cc. xylene, the mixture refluxed 48 hrs., cooled, treated with H₂O, the aqueous layer extracted with Et₂O, the joined organic solns. washed, dried, and evaporated to yield 12 g. crude 3-ethyl-10-{γ-(2-tetrahydropyranyloxy)propyl}phenoxazine, b_{0.5} 230°. This is dissolved in 80 cc. 75% aqueous EtOH containing 1.5 cc. concentrated HCl and refluxed 1 hr., after evaporation the residue suspended in Et₂O and neutralized with NaHCO₃, filtered, dried, and distilled to yield 7 g. 3-ethyl-10-(γ-hydroxypropyl)phenoxazine, b_{0.5} 210°, m. 37-40°. This is refluxed 1 hr. with 12 g. PBr₃ in 20 cc. CHCl₃, cooled, stirred with NaHSO₃ before washing with NaHCO₃, the organic layer dried, and evaporated to yield 9 g. crude III. Preparation of 3-ethyl-10-(β-piperidinopropyl)phenoxazine (IV): II (8.4 g.), 1.56 g. NaNH₂, and 25 cc. toluene is refluxed and stirred 45 min., cooled before addition of 2.9 g. propylene oxide, the mixture stirred at 20° 5 hrs., left overnight, treated with H₂O, the aqueous layer extracted with C₆H₆, the joined organic solns. dried, and distilled to yield 5.35 g. 3-ethyl-10-(β-hydroxypropyl)phenoxazine (IVa), b_{0.4} 190°. p-Toluenesulfonyl chloride (9.32 g.) in 20 cc. pyridine is slowly added with stirring at 0° to 12.46 g. IVa in 15 cc. pyridine, after 1 night at room temperature 500 cc. H₂O added, the oil washed with H₂O, dissolved in C₆H₆, the solution dried before evaporation, and the oily residue crystallized slowly to yield 11 g. β-[α-(3-ethyl-10-phenoxaziny)propyl] p-toluenesulfonate (IVb), m. 87-90°, after washing with EtOH and drying. IVb (5 g.) and 2 g. piperidine in 30 cc. propanol is heated at 100° 40 hrs., after evaporation the residue treated with H₂O and Et₂O, the ether solution washed with 10% NaOH then H₂O, extracted with N/10 HCl, made alkaline with NaOH, extracted with Et₂O, the organic solution dried, and distilled to yield 1.35 g. IV, b_{0.5} 200°; IV hydrochloride m. 201-3° (absolute EtOH). 3-Ethyl-10-(β-diethylaminopropyl)phenoxazine, b_{0.3} 180°, is similarly prepared; hydrochloride m. 176-80° 3-Acetylphenoxazine-10-carboxylic acid β-pyrrolidinoethyl ester hydrochloride is prepared by refluxing 5.75 g. 3-acetylphenoxazine-10-carboxylic acid chloride and 2.4 g. pyrrolidinoethanol in 20 cc. C₆H₆, during 15 hrs. After cooling the precipitate is treated with 50 cc. Et₂O to yield 5.03 g. product, m. 181-3° (decomposition) (acetone and drying in vacuum at 80° in the presence of P₂O₅). This procedure is applied to the preparation of the following compds.: 3-acetylphenoxazine-10-carboxylic acid γ-diethylaminopropyl ester

hydrochloride, m. 141-2°; 3-acetylphenoxazine-10-carboxylic acid γ -dimethylaminopropyl ester hydrochloride (V), m. 126-30°; 3-acetylphenoxazine-10-carboxylic acid γ -pyrrolidinopropyl ester hydrochloride, m. 141-3°. 3-Acetyl-10-(γ -dimethylaminopropyl)phenoxazine hydrochloride (VI) is prepared as follows. V (6.9 g.) and 80 cc. H₂O is washed with Et₂O, made alkaline with NaOH, extracted with Et₂O, the ether solution washed, dried, and evaporated to afford the ester, m. 63°. After decarboxylation at 200°/16 mm. and distillation, the oil, b0.2 220°, is dissolved in Et₂, the solution filtered, extracted with 50 cc. N/3 HCl, washed with H₂O, the aqueous solns. made alkaline, extracted with Et₂O, the organic solns. dried, evaporated, and the residue treated by HCl gas in EtOH-Et₂O to yield 4.2 g. VI, m. 246-7°. 3-Acetyl-10-(γ -pyrrolidinopropyl)phenoxazine hydrochloride, m. 215-16°, is similarly prepared 3-Acetyl-10-(γ -pyrrolidinoethyl)phenoxazine hydrochloride, m. 226-8°, is obtained in 4.4-g. yield by refluxing 6 hrs. 5.75 g. 3-acetylphenoxazine-10-carboxylic acid chloride and 5 g. pyrrolidinoethanol in 20 cc. C₆H₆, by decarboxylating the product at 200°, and by treating the oil, b0.5, 230°, as in the previous procedure. The following products are similarly prepared: 3-acetyl-10-(γ -dimethylaminopropyl)phenoxazine, b0.4 225°, hydrochloride, m. 246-7° (absolute EtOH); 3-acetyl-10-(γ -diethylaminopropyl)phenoxazine, b0.2 220°, hydrochloride, m. 173-4°; 3-acetyl-10-[γ -(N'-methylpiperazino)propyl]phenoxazine, b0.2 240°, di-HCl salt, m. 270-1° (decomposition); 3-acetyl-10-(γ -dimethylamino- β -methylpropyl)phenoxazine, b3 210°; hydrochloride, m. 224-5°; 3-acetyl-10-(γ -pyrrolidino- β -methylpropyl)phenoxazine, b0.5 230°, hydrochloride, m. 200° (decomposition); 3-acetyl-10-[γ -(N'-methylpiperazino)- β -methylpropyl]phenoxazine, b0.4 240°, di-HCl salt, m. 242-4° (decomposition).

- IT 95623-30-6, Phenoxazine-10-ethanol, 2-ethyl- α -methyl-,
p-toluenesulfonate
(preparation of)
RN 95623-30-6 CAPLUS
CN Phenoxazine-10-ethanol, 2-ethyl- α -methyl-, p-toluenesulfonate (6CI,
7CI) (CA INDEX NAME)



L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN
 AN 1960:2359 CAPLUS Full-text
 DN 54:2359
 OREF 54:586d-i
 TI Phenoxazine compounds
 PA Recherche et industrie therapeutiques R.I.T., S.A.
 DT Patent
 LA Unavailable

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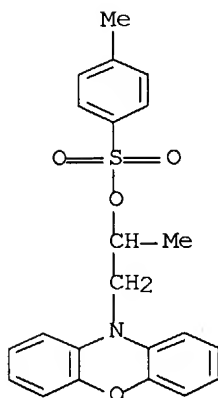
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	BE 569697		19590124	BE	
AB	<p>Preparation of new anesthetics and analgesics, potentiators and deconnectors of the vegetative nervous system was described. Phenoxazine (7.32 g.) and 1.56 g. NaNH₂ in 20 cc. anhydrous toluene was refluxed with stirring during 1 hr., 15 cc. toluene containing α-chloro-γ-dimethylaminopropane (prepared from 7 g. corresponding HCl salt) added, after 2 hrs. refluxing the mixture cooled, treated with 30 cc. H₂O, the aqueous phase extracted with C₆H₆, the organic solns. dried, evaporated, the residue dissolved in 100 cc. ligroine (b. 40-60°), the insol. phenoxazine recovered, and the solution distilled in vacuo to yield 6.3 g. oil, b0.5 190°, treated with HCl-absolute EtOH then Et₂O to yield 5.85 g. crude 10-(γ-dimethylaminopropyl)phenoxazine hydrochloride (I), m. 132-4° (Me₂CO). Similarly prepared were: 10-(β-diethylaminoethyl)phenoxazine hydrochloride, m. 167-9° (base b1 190°); 10-(β-pyrrolidinoethyl)phenoxazine hydrochloride, m. 203-5° (base b0.2-0.3 170°); 10-(β-morpholinoethyl)phenoxazine hydrochloride, m. 226-7° (base b1-2 170°); 10-(γ-diethylaminopropyl)phenoxazine H succinate, m. 112-15° [picrate m. 138-42° (decomposition)]; 10-(γ-pyrrolidinopropyl)phenoxazine hydrochloride (II), m. 162-3° (base b3 220°); 10-(γ-pyrrolidino-β-methylpropyl)-phenoxazine hydrochloride, m. 170-1° (base b0.8 200°); 10-(γ-diethylamino-β-methylpropyl)phenoxazine hydrochloride, m. 156-8° (base b0.5 190°); 10-(β-dimethylaminopropyl)phenoxazine picrate, m. 154-5° (decomposition), and hydrochloride, m. 175-7° (base b1-2 160-70°); 10-(β-diethylaminopropyl)phenoxazine hydrochloride, m. 208-10° [base b1 180°; picrate m. 152-3° (decomposition)]; 10-(β-diethylaminoisopropyl)phenoxazine hydrochloride, m. 162-4° [picrate m. 152-3° (decomposition)]; 10-(β-hydroxypropyl)phenoxazine, b0.5 195°, m. 95-8° (p-toluenesulfonate m. 136-8°); 10-(β-pyrrolidinopropyl)phenoxazine hydrochloride, m. 198-201°; 10-(γ-piperidinopropyl)phenoxazine hydrochloride (III), m. 197° (Et₂O-alc.), from Et β-(10-phenoxazinyl)propionate, b2 210°, via 10-(γ-hydroxypropyl)phenoxazine, b0.8 200°, and γ-[α-(10-phenoxazinyl)]-propyl p-toluenesulfonate, m. 52-4° and 158°. Phenoxazine (7.32 g.) was added to 1.01 g. Na in 40 cc. NH₄OH containing 1 crystal Fe(NO₃)₃, the mixture stirred 15 min., 6.3 g. α-bromo-γ-chloropropane slowly added, the NH₃ evaporated, the residue treated with H₂O, extracted with Et₂O, the ether evaporated, 25 cc. anhydrous toluene, powdered Fe, and 5.68 g. pyrrolidine added to the residue, the mixture heated at 100-10° 48 hrs., after H₂O extraction the organic layer dried, and distilled to yield 7.6 g. base, b0.5 190°, converted into 6.8 g. II, m. 160-2°. The same procedure with piperidine yielded III, m. 197-9°, with Pr₂NH yielded 10-[γ-(di-n-propylamino)propyl]phenoxazine, b1 210° (hydrochloride m. 152-</p>				

3°), with morpholine yielded 10-(γ-morpholinopropyl)phenoxazine, b1
230° (hydrochloride m. 195-6°).

IT **95137-74-9**, Phenoxazine-10-ethanol, α-methyl-,
p-toluenesulfonate **95137-75-0**, Phenoxazine-10-propanol,
p-toluenesulfonate
(preparation of)

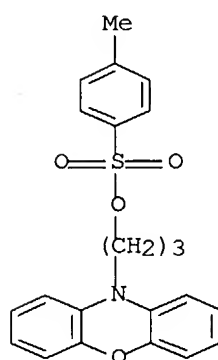
RN 95137-74-9 CAPLUS

CN Phenoxazine-10-ethanol, α-methyl-, p-toluenesulfonate (6CI, 7CI)
(CA INDEX NAME)

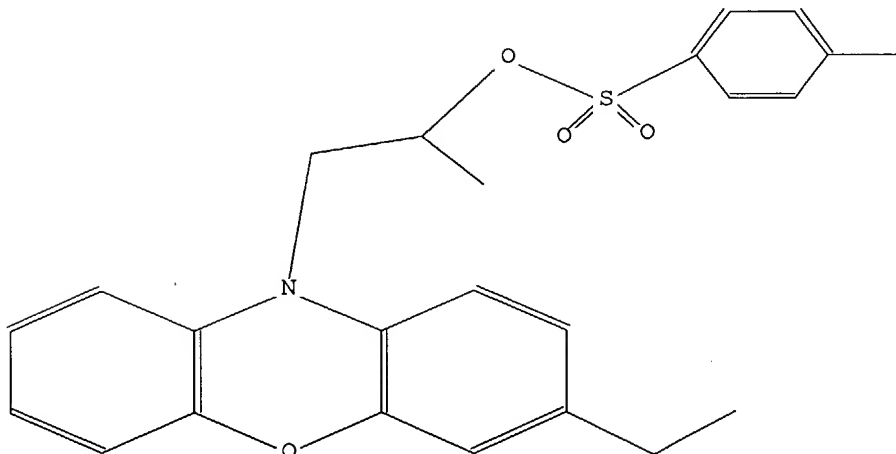


RN 95137-75-0 CAPLUS

CN Phenoxazine-10-propanol, p-toluenesulfonate (6CI, 7CI) (CA INDEX NAME)



Beilstein Records (BRN):	722152
Chemical Name (CN):	1-(3-ethyl-phenoxazin-10-yl)-2-(toluene-4-sulfonyloxy)-propane
Autonom Name (AUN):	toluene-4-sulfonic acid 2-(3-ethyl-phenoxazin-10-yl)-1-methyl-ethyl ester
Molec. Formula (MF):	C24 H25 N O4 S
Molecular Weight (MW):	423.53
Lawson Number (LN):	30943, 13813, 3132
Compound Type (CTYPE):	heterocyclic
Constitution ID (CONSID):	719862
Tautomer ID (TAUTID):	748666
Beilstein Citation (BSO):	5-27
Entry Date (DED):	1988/11/28
Update Date (DUPD):	1992/08/10



1. Patent: R.I.T. BE 575133, Chem.Abstr.(5708), <1960>

L10 ANSWER 1 OF 11 MARPAT COPYRIGHT 2004 ACS on STN

AN 137:201319 MARPAT Full-text

TI Preparation of β -aryl- α -oxy substituted alkylcarboxylic acids as hypolipidemic, antihyperglycemic, antiobesity, and hypocholesterolemic agents

IN Lohray, Braj Bhushan; Lohray, Vidya Bhushan; Bajji, Ashok Channaveerappa; Kalchar, Shivaramayya; Paraselli, Rao Bheema; Gurram, Ranga Madhavan; Ramanujam, Rajagopalan; Chakrabarti, Ranjan

PA Reddy's Research Foundation, India; Reddy-Cheminor, Inc.

SO U.S., 43 pp., Cont.-in-part of U.S. 6,054,453.

CODEN: USXXAM

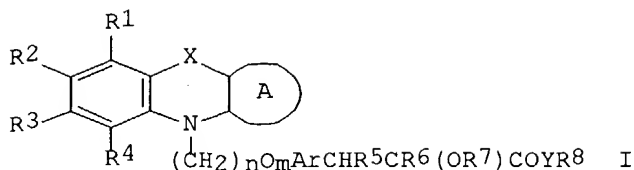
DT Patent

LA English

FAN.CNT 4

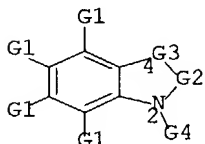
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6440961	B1	20020827	US 1999-257104	19990224
	US 6054453	A	20000425	US 1998-12585	19980123
	GB 2380997	A1	20030423	GB 2002-30280	19980123
	GB 2380997	B2	20030702		
	WO 2000050414	A1	20000831	WO 1999-IB683	19990416
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9929537	A1	20000914	AU 1999-29537	19990416
	NZ 513689	A	20010928	NZ 1999-513689	19990416
	EP 1155006	A1	20011121	EP 1999-910638	19990416
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	TR 200103218	T2	20020321	TR 2001-200103218	19990416
	BR 9917155	A	20020423	BR 1999-17155	19990416
	JP 2002537390	T2	20021105	JP 2000-600997	19990416
	EE 200100446	A	20021216	EE 2001-446	19990416
	US 6548666	B1	20030415	US 2001-853176	20010510
	US 6608194	B1	20030819	US 2001-853177	20010510
	HR 2001000612	A1	20021231	HR 2001-612	20010822
	NO 2001004102	A	20011024	NO 2001-4102	20010823
	ZA 2001006994	A	20031125	ZA 2001-6994	20010823
	BG 105925	A	20020628	BG 2001-105925	20010920
PRAI	IN 1997-MA2416		19971027		
	US 1998-12585		19980123		
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	WO 1999-IB683		19990416		

GI

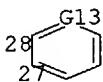


AB β -Aryl- α -oxy substituted alkylcarboxylic acids I [R1-4 = H, halo, OH, NO₂, CN, CHO, etc.; A = 5-6 membered (hetero)cycle; X = O, S; Ar = (un)substituted divalent aromatic or heterocyclic group; R5 = H, OH, alkoxy, halo, alkyl; R6 = H, OH, alkoxy, halo, alkyl group, acyl, (un)substituted aralkyl or forms a bond together with R5; R7 = H, (un)substituted alkyl, cycloalkyl, aryl, aralkyl, etc.; R8 = H, alkyl, cycloalkyl, aryl, aralkyl, etc.; Y = O, NR₁₀; R₁₀ = H, alkyl, aryl, hydroxyalkyl, aralkyl, heterocyclyl, heteroaryl, heteroaralkyl groups; R8, R₁₀ together form a 5 or 6 membered (hetero)cycle; n = 1-4; m = 0-1] were prepared E.g., 3-[4-[2-(phenoxazinyl)ethoxy]phenyl]-2-hydroxypropanoic acid was prepared Example compds. were shown to possess peroxisome proliferator activated receptors, PPAR- α and PPAR- γ and shown to inhibit HMG CoA reductase. I are used to treat diabetes caused by insulin resistance.

MSTR 1



G2 = 28-4 27-2



G3 = O
G6 = (1-4) CH₂
G13 = CH
G21 = 327

³Q₇—SO₂—G41

G41 = p-C₆H₄Me
DER: or pharmaceutically acceptable solvates
MPL: claim 1
NTE: substitution is restricted
NTE: or derivatives, analogs, tautomeric forms and polymorphs
NTE: also incorporates claims 26, 27, 35 and 37
STE: or stereoisomers

RE.CNT 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 11 MARPAT COPYRIGHT 2004 ACS on STN

AN 133:193155 MARPAT Full-text

TI Preparation of β -aryl- α -oxy substituted alkylcarboxylic acids
as hypolipidemic, antihyperglycemic, antiobesity, and
hypocholesterolemic

agents

IN Lohray, Braj Bhushan; Lohray, Vidya Bhushan; Ashok, Channaveerappa
Bajji;

Shivaramayya, Kalchar; Paraselli, Bheema Rao; Gurram, Ranga Madhavan;
Rajagopalan, Ramanujam; Rajan, Chakrabarti

PA Dr.Reddy's Research Foundation, India

SO PCT Int. Appl., 116 pp.

CODEN: PIXXD2

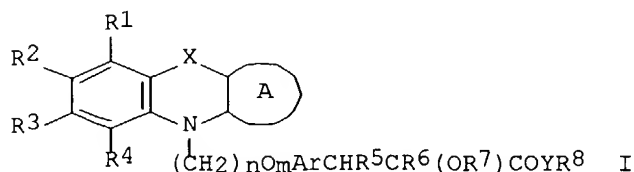
DT Patent

LA English

FAN.CNT 4

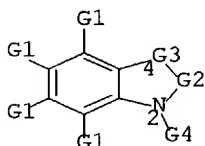
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000050414	A1	20000831	WO 1999-IB683	19990416
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
	GB 2380997	A1	20030423	GB 2002-30280	19980123
	GB 2380997	B2	20030702		
	US 6440961	B1	20020827	US 1999-257104	19990224
	AU 9929537	A1	20000914	AU 1999-29537	19990416
	EP 1155006	A1	20011121	EP 1999-910638	19990416
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO			
	BR 9917155	A	20020423	BR 1999-17155	19990416
	JP 2002537390	T2	20021105	JP 2000-600997	19990416
	EE 200100446	A	20021216	EE 2001-446	19990416
	HR 2001000612	A1	20021231	HR 2001-612	20010822
	NO 2001004102	A	20011024	NO 2001-4102	20010823
	BG 105925	A	20020628	BG 2001-105925	20010920
PRAI	US 1999-257104		19990224		
	IN 1997-MA2416		19971027		
	GB 2000-10176		19980123		
	US 1998-12585		19980123		
	WO 1999-IB683		19990416		

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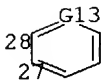


AB β -Aryl- α -oxy substituted alkylcarboxylic acids I [R1-R4 = H, halo, OH, NO2, etc.; ring A = 5-6 membered cyclic structure containing C atoms and may contain O, S, N; X = O, S, NR9; Ar = aromatic or heterocyclic group; R5 = H, LH, alkoxy, etc.; R6 = H, OH, halo, etc.; R7 = H, alkyl, aryl, etc.; R8 = H, alkyl, cycloalkyl, etc.; Y = O, NR10; n = 1-4; m = 0, 1], hypolipidemic, antihyperglycemic, antiobesity and hypocholesterolemic agents, were prepared E.g., 3-[4-[2-(phenoxazin-10-yl)ethoxy]phenyl]-2-hydroxypropanoic acid was prepared

MSTR 1



G2 = 28-4 27-2



G3 = O
G6 = (1-4) CH2
G13 = CH
G21 = 327

³Q₂₇-SO₂-G41

G41 = p-C₆H₄Me
DER: or pharmaceutically acceptable solvates
MPL: claim 1
NTE: substitution is restricted
NTE: or derivatives, analogs, tautomeric forms and polymorphs
NTE: also incorporates claims 26, 27, 35 and 37
STE: or stereoisomers

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 11 MARPAT COPYRIGHT 2004 ACS on STN

AN 131:44742 MARPAT Full-text

TI Preparation and antiinflammatory activity of N-substituted
azaheterocyclic
compounds

IN Joergensen, Tine Krogh; Fischer, Erik; Hohlweg, Rolf; Andersen, Knud
Erik;

Olsen, Uffe Bang; Sindelar, Karel; Silhankova, Alexandra; Konigova,
Otylie; Polivka, Zdenek

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 52 pp.

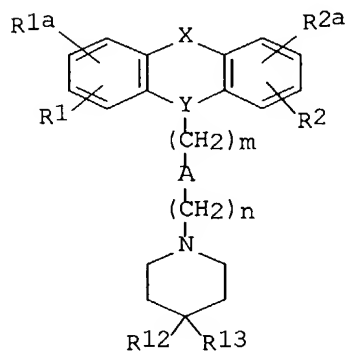
CODEN: PIXXD2

DT Patent

LA English

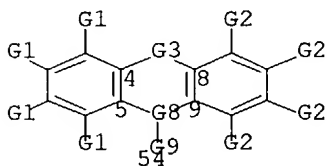
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9931058	A1	19990624	WO 1998-DK550	19981214
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ,			
TM		RW:	GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		
	AU 9916629	A1	19990705	AU 1999-16629	19981214
	US 6048856	A	20000411	US 1998-211378	19981214
	EP 1047673	A1	20001102	EP 1998-961079	19981214
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,			
FI	JP 2002508353	T2	20020319	JP 2000-538985	19981214
PRAI	DK 1997-1472		19971217		
	US 1997-82049		19971218		
	WO 1998-DK550		19981214		
GI					



AB N-substituted azaheterocyclic compds. I [R1, R1a, R2, R2a = H, halo, cyano, OH, etc.; X = o-phenylene, O, S, CH2CH2, etc.; Y = N, CN, N(CO), etc.; A = C.tplbond.C, CO, C(:CH2), etc.; R12 = H, hydroxyalkyl, etc.; R13 = cyano, amino, etc.; m, n = 0-2], useful for clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation as well as their use for treatment of indications caused by or related to the secretion and circulation of insulin antagonizing peptides, e.g. non-insulin-dependent diabetes mellitus (NIDDM) and ageing-associated obesity, were prepared E.g., 1-(3-(10,11-dihydro-5H-dibenzo[a,d]cyclohepten- 5-ylidene)-1-propyl)-4-phenyl-4-piperidinecarboxylic acid was prepared

MSTR 1



G3 = O
G8 = 163-5 164-54 163-9

$\text{N} \xrightarrow{163-164} \text{G10}$

G9 = 157

$\text{Q} \xrightarrow{157} \text{SO}_2 \text{---} \text{G31}$

G10 = C(O)
G31 = p-C6H4Me
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: also incorporates claim 13

RE.CNT 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 11 MARPAT COPYRIGHT 2004 ACS on STN

AN 128:294711 MARPAT Full-text

TI Preparation of N-substituted azaheterocyclic compounds as analgesics and antiinflammatories

IN Jorgensen, Tine Krogh; Hohlweg, Rolf; Madsen, Peter; Andersen, Knud Erik;

Treppendahl, Svend; Olsen, Uffe Bang; Polivka, Zdenek; Silhankova, Alexandra; Sindelar, Karel; Valenta, Vladimir; Kalisz, Tomas

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 86 pp.

CODEN: PIXXD2

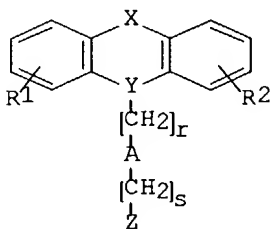
DT Patent

LA English

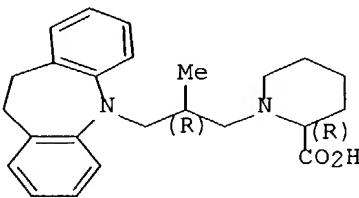
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9815546	A1	19980416	WO 1997-DK421	19971002
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	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9743771	A1	19980505	AU 1997-43771	19971002
	AU 741839	B2	20011213		
	EP 934306	A1	19990811	EP 1997-941883	19971002
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO			
	BR 9712202	A	19990831	BR 1997-12202	19971002
	CN 1234797	A	19991110	CN 1997-199183	19971002
	JP 2001501629	T2	20010206	JP 1998-517092	19971002
	US 6569849	B1	20030527	US 1997-943856	19971003
	NO 9901563	A	19990603	NO 1999-1563	19990330
	KR 2000048909	A	20000725	KR 1999-702939	19990403
PRAI	DK 1996-1089		19961004		
	WO 1997-DK421		19971002		

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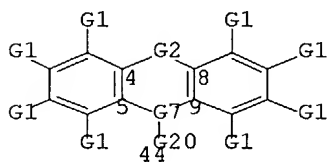


II

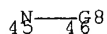
AB The title compds. [I; R1, R2 = H, halo, CF3, etc.; X = o-phenylene, O, S, etc.; Y = N, CH, N(C:O), C:C(R8) (only first atom participates in the ring system and R8 = H, C1-6 alkyl); A = C.tplbond.C, C(O), C:CH, etc.; r, s = 0-4; Z = substituted piperidino, piperazino, pyrrolidino, etc.]

and their salts, useful for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation as well as useful for treatment of indications caused by or related to secretion and circulation of insulin antagonizing peptides, were prepared and formulated. Thus, reaction of iminodibenzyl with [3-bromo-2(R)-methylpropoxy]tetrahydropyran in the presence of NaNH₂ in C₆H₆ followed by methanesulfonylation of the resulting 3-(10,11-dihydro-5H-dibenzo[b,f]azepin-5-yl)-(2S)-methyl-1- propanol, reaction of the methanesulfonate with (R)-2-piperidinecarboxylic acid Et ester hydrochloride in the presence of K₂CO₃ in DMF, and hydrolysis of the resulting ester with 5N NaOH afforded the title compound II.HCl with showed 47% inhibition of histamine induced pain response at 1.0 mg/kg.

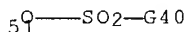
MSTR 1A



G2 = O
G7 = 45-5 46-44 45-9



G8 = alkenylene<EC (2-16) C, BD (1) D>
(SO (1) cycloalkyl<(3-7)>)
G20 = 51



G40 = p-C₆H₄Me
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted
NTE: also incorporates claim 16

RE.CNT 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

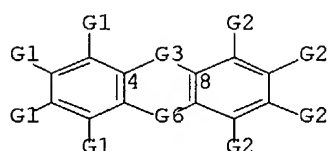
L10 ANSWER 5 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
 AN 128:282847 MARPAT Full-text
 TI Preparation of 1,4-disubstituted piperazines for the treatment of
 painful,
 hyperalgesic and/or inflammatory conditions
 IN Hohlweg, Rolf; Madsen, Peter; Jorgensen, Tine Krogh; Andersen, Knud
 Erik;
 Watson, Brett; Polivka, Zdenek; Konigova, Otylie; Kovandova, Martina;
 Silhankova, Alexandra; Valenta, Vladimir
 PA Novo Nordisk A/S, Den.
 SO PCT Int. Appl., 59 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9815548	A1	19980416	WO 1997-DK422	19971002
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	RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
	AU 9743772	A1	19980505	AU 1997-43772	19971002
	AU 740662	B2	20011108		
	EP 934312	A1	19990811	EP 1997-941884	19971002
	EP 934312	B1	20030319		
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO			
	BR 9712196	A	19990831	BR 1997-12196	19971002
	CN 1234799	A	19991110	CN 1997-199184	19971002
	CN 1088459	B	20020731		
	JP 2001502307	T2	20010220	JP 1998-517093	19971002
	RU 2188197	C2	20020827	RU 1999-109024	19971002
	AT 234831	E	20030415	AT 1997-941884	19971002
	ES 2194217	T3	20031116	ES 1997-941884	19971002
	ZA 9708864	A	19980406	ZA 1997-8864	19971003
	US 5916889	A	19990629	US 1997-943726	19971003
	US 6004961	A	19991221	US 1999-271785	19990318
	US 6040302	A	20000321	US 1999-271565	19990318
	US 6133268	A	20001017	US 1999-271564	19990318
	NO 9901565	A	19990604	NO 1999-1565	19990330
	KR 2000048899	A	20000725	KR 1999-702928	19990403
PRAI	DK 1996-1090		19961004		
	WO 1997-DK422		19971002		
	US 1997-943726		19971003		
GI					

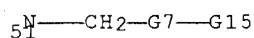
* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB The title compds. [I; R1, R2 = H, halo, CF3, etc.; X = o-phenylene, O, S, etc.; Y = N-CH2-, CH-CH2-, C:CH-, CH-O- (only the first atom participates in the ring system); r = 1-3; Z = II-V (M1, M2 = C, N; R5 = H, C1-6 alkyl, PhCH2, Ph; R3 = H, halo, CF3, NO2, CN; R4 = H, halo, CF3, etc.)] and their salts, useful for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role such as e.g. neurogenic pain, inflammation, migraine, neuropathy, itching and rheumatoid arthritis, as well as for the treatment of indications caused by or related to the secretion and circulation of insulin antagonizing peptides, e.g. non-insulin-dependent diabetes mellitus (NIDDM) and ageing-associated obesity, were prepared and formulated. Thus, reaction of 6-(1-piperazinyl)-2-pyridinecarboxylic acid Et ester (preparation described) with (10,11-dihydro-5H-dibenzo[b,f]acepin-5-yl)-1-Pr methanesulfonate in the presence of K2CO3 in Me2CO followed by hydrolysis of the resulting ester with NaOH in H2O/EtOH afforded the title compound VI.HCl which showed 61% inhibition of histamine induced pain response at 1.0 mg/kg.

MSTR 1



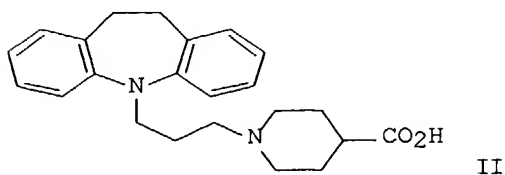
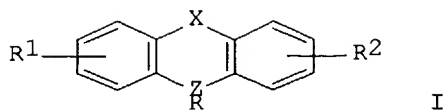
G3 = O
G6 = 51



G7 = (1-3) CH2
G15 = OSO2C6H4Me-p
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted
NTE: also incorporates claim 12

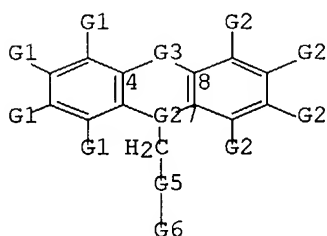
L10 ANSWER 6 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
 AN 126:8010 MARPAT Full-text
 TI Preparation of N-(3-dibenzazepinopropyl)piperidinecarboxylates and
 analogs
 as drugs
 IN Doerwald, Florenzio Zaragossa; Andersen, Knud Erik; Madsen, Peter;
 Joergensen, Tine Krogh; Hohlweg, Rolf; Andersen, Henrik Sune;
 Tréppendahl,
 Svend; Olsen, Uffe Bang; Zdenek, Polivka; et al.
 PA Novo Nordisk A/s, Den.
 SO PCT Int. Appl., 85 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9631498	A1	19961010	WO 1996-DK139	19960401
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
	CA 2217197	AA	19961010	CA 1996-2217197	19960401
	AU 9651003	A1	19961023	AU 1996-51003	19960401
	AU 708010	B2	19990729		
	EP 820451	A1	19980128	EP 1996-907327	19960401
	EP 820451	B1	20030115		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI				
	BR 9604864	A	19980526	BR 1996-4864	19960401
	CN 1183781	A	19980603	CN 1996-193779	19960401
	JP 11503127	T2	19990323	JP 1996-529868	19960401
	CZ 291294	B6	20030115	CZ 1997-3164	19960401
	AT 231144	E	20030215	AT 1996-907327	19960401
	ES 2191090	T3	20030901	ES 1996-907327	19960401
	PL 187171	B1	20040531	PL 1996-322722	19960401
	IL 117810	A1	20010913	IL 1996-117810	19960403
	ZA 9602732	A	19961024	ZA 1996-2732	19960404
	TW 419463	B	20010121	TW 1996-85104810	19960514
	NO 9704605	A	19971204	NO 1997-4605	19971006
PRAI	DK 1995-405		19950407		
	DK 1995-1005		19950911		
	WO 1996-DK139		19960401		
GI					



AB Title compds. [I; R = N-attached carboxyheterocyclyl, etc.; R1,R2 = H, halo, alkyl, alkoxy, etc.; X = O, CH2CH2, CH2CO, etc.; Z = N(CH2)2-4, CH(CH2)2-4, CH:CH(CH2)1-3] were prepared for treatment of neurogenic inflammation and non-insulin-dependant diabetes (no data). Thus, 10,11-dihydro-5H-dibenz[b,f]azepine was acylated by Cl(CH2)3COCl and the reduced product aminated by Et 4-piperidinecarboxylate to give, after saponification, title compound II.HCl.

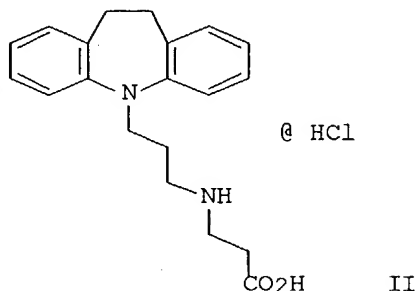
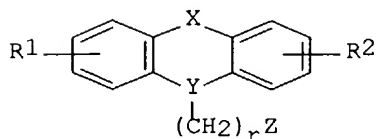
MSTR 1A



G3 = O
 G5 = (1-3) CH2
 G6 = OSO2C6H4Me-p
 G27 = N
 DER: or pharmaceutically acceptable salts
 MPL: claim 1
 NTE: substitution is restricted
 NTE: also incorporates claim 25

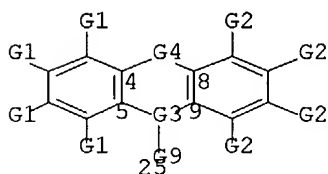
L10 ANSWER 7 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
 AN 125:328528 MARPAT Full-text
 TI Preparation of heterocyclic tricyclic analgesics, antidiabetics and
 antiinflammatory agents
 IN Madsen, Peter; Andersen, Knud Erik; Doerwald, Florenzio Zaragossa;
 Joergensen, Tine Krogh; Andersen, Henrik Sune; Hohlweg, Rolf; Olsen,
 Uffe
 Bang
 PA Novo Nordisk A/s, Den.
 SO PCT Int. Appl., 43 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9631481	A1	19961010	WO 1996-DK141	19960401
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
	US 5962449	A	19991005	US 1996-623447	19960328
	CA 2217198	AA	19961010	CA 1996-2217198	19960401
	AU 9652706	A1	19961023	AU 1996-52706	19960401
	EP 820443	A1	19980128	EP 1996-909078	19960401
	EP 820443	B1	20010919		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE,				
FI	JP 11503129	T2	19990323	JP 1996-529870	19960401
	AT 205833	E	20011015	AT 1996-909078	19960401
	ZA 9602733	A	19961024	ZA 1996-2733	19960404
PRAI	DK 1995-407		19950407		
	DK 1995-1002		19950911		
	WO 1996-DK141		19960401		
GI					

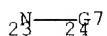


AB The title compds. [I; R1, R2 = H, halogen, CF3, OH, alkyl, alkoxy; X = O, S, CH2CH2, (un)substituted NH, CH2O, OCH2, S(:O), etc.; Y = NCH2, CHCH2, C:CH; Z = (un)substituted 2-pyridylamino, (un)substituted cyclohexylamino, etc.; r = 1-3], useful for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation, and for the treatment of noninsulin-dependent diabetes mellitus (no data), are prepared and a I-containing formulation presented. Thus, dihydrodibenz[b,f]azepine II (m.p. 114-117°) was prepared in 4 steps from 10,11-dihydro-5H- dibenz[b,f]azepine and demonstrated a 36% inhibition of pain in a mouse formalin-induced pain model at 0.1 mg/kg.

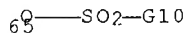
MSTR 2



G3 = 23-5 23-9 24-25



G4 = O
G7 = (2-4) CH2
G9 = 65



G10 = p-C6H4Me
MPL: claim 27

L10 ANSWER 8 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
 AN 125:328521 MARPAT Full-text
 TI Preparation of N-heterocyclalkyl-substituted 3-pyridinecarboxylic
 acids

and esters for treatment of neurogenic inflammation and insulin
 resistance

in NIDDM or aging

IN Andersen, Henrik Sune; Andersen, Knud Erik; Madsen, Peter; Joergensen,
 Tine Krogh; Hohlweg, Rolf; Petersen, Hans; Olsen, Uffe Bang

PA Novo Nordisk A/s, Den.

SO PCT Int. Appl., 55 pp.

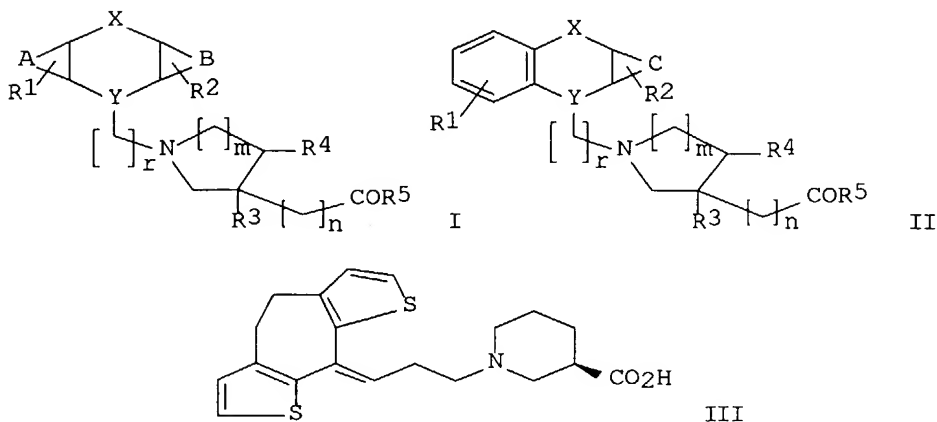
CODEN: PIXXD2

DT Patent

LA English

FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9631469	A1	19961010	WO 1996-DK142	19960401
	W:				
	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,				
	ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT,				
	LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,				
	SG, SI				
	RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR,				
	IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML				
	AU 9652707	A1	19961023	AU 1996-52707	19960401
	ZA 9602737	A	19961017	ZA 1996-2737	19960404
PRAI	DK 1995-402		19950407		
	DK 1995-404		19950407		
	DK 1995-408		19950407		
	DK 1995-1004		19950911		
	DK 1995-1007		19950911		
	WO 1996-DK142		19960401		
OS	CASREACT 125:328521				
GI					



AB The title compds. [I and II; R1, R2 = H, halo, CF3, etc.; A together with the double bond = benzene, pyridine, pyrimidine, etc.; B together with the double bond = pyridine, pyrimidine, pyrazine, etc.; C together with the double bond = bicyclic system such as naphthalene, quinoline, isoquinoline, etc.; Y = N(CH2-), CH(CH2-), C(:CH-) (wherein only the first atom participates in the ring system); X = O, S, (CH2)2, etc.; R3, R4 = H, bond; R5 = OH, C1-6 alkoxy; r = 1-3; m = 1-2; n = 1 when m = 1; n = 0 when m = 2], useful for the clin. treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation, were prepared and formulated. Thus, treatment of 3-{4,5-dihydrocyclohepta[2,1-b;4,5-b']dithiophen-9-ylidene}-1-propanol with MeSO2Cl in the presence of Et3N in CH2Cl2 followed by reaction of the resulting methanesulfonate with (R)-(-) Et 3-pyridinecarboxylate (L)-(+)-tartrate in the presence of Li2CO3 in iPrOAc and hydrolysis of the ester group afforded the expected product (R)-III.HCl which showed 34% inhibition of formalin induced pain response at 0.1 mg/kg in mice.

MSTR 1B

G22-~~G3~~^{G5}-G17

G3 = O
G4 = 35-4 36-23 35-8

~~G9~~^{G9}-~~G3~~^{G6}CH2

G5 = (1-3) CH2
G9 = N
G11 = o-C6H4 (SO G1)
G12 = o-C6H4 (SO G1)
G17 = OSO2C6H4Me-p
DER: or pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted
NTE: also incorporates claim 27

L10 ANSWER 9 OF 11 MARPAT COPYRIGHT 2004 ACS on STN

AN 123:313776 MARPAT Full-text

TI Novel azaheterocyclic acids useful as analgesics and antiinflammatories.

IN Andersen, Knud Erik; Olsen, Uffe Bang; Petersen, Hans; Groenvald, Frederik

Christian; Sonnewald, Ursula; Joergensen, Tine Krogh; Andersen, Henrik Sune

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 54 pp.

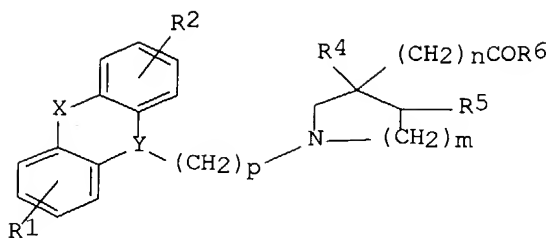
CODEN: PIXXD2

DT Patent

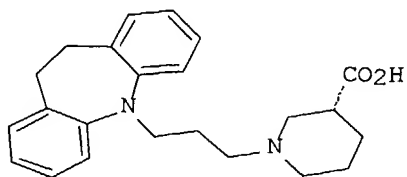
LA English

FAN.CNT 5

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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PI	WO 9518793	A1	19950713	WO 1995-DK2	19950103
	W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MW, MX, NO, NZ, PL, RO, RU, SD, SI, SK, TJ, TT, UA, UZ, VN				
	RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	IL 112222	A1	19991231	IL 1995-112222	19950102
	CA 2180238	AA	19950713	CA 1995-2180238	19950103
	AU 9513110	A1	19950801	AU 1995-13110	19950103
	AU 691858	B2	19980528		
	EP 738262	A1	19961023	EP 1995-904409	19950103
	EP 738262	B1	20000419		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
SE	CN 1142226	A	19970205	CN 1995-191845	19950103
	CN 1083431	B	20020424		
	HU 75878	A2	19970528	HU 1996-1842	19950103
	JP 09507239	T2	19970722	JP 1995-518275	19950103
	JP 2944221	B2	19990830		
	BR 9506452	A	19970902	BR 1995-6452	19950103
	CZ 286109	B6	20000112	CZ 1996-1921	19950103
	AT 191909	E	20000515	AT 1995-904409	19950103
	ES 2147837	T3	20001001	ES 1995-904409	19950103
	PT 738262	T	20001031	PT 1995-904409	19950103
	PL 180209	B1	20010131	PL 1995-315294	19950103
	RU 2167152	C2	20010520	RU 1996-116134	19950103
	NZ 277763	A	20011130	NZ 1995-277763	19950103
	ZA 9500031	A	19960704	ZA 1995-31	19950104
	NO 9602811	A	19960904	NO 1996-2811	19960703
	FI 9602749	A	19960904	FI 1996-2749	19960704
	GR 3033967	T3	20001130	GR 2000-401652	20000717
PRAI	DK 1994-19		19940104		
	DK 1994-1290		19941109		
	WO 1995-DK2		19950103		
OS	CASREACT 123:313776				
GI					



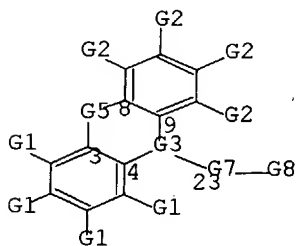
I



II

AB The invention relates to novel N-substituted azaheterocyclic carboxylic acids and esters I [R1, R2 = H, halo, CF3, alkyl, alkoxy; Y = NCH2, CHCH2, or C:CH, where only the 1st atom is within the ring; X = O, S, CR7R8, CH2CH2, CH:CHCH2, CH2CH:CH, CH2CH2CH2, CH:CH, NR9CO, OCH2, CO, SO; R7, R8, R9 = H, alkyl; p = 1, 2, 3; m = 1, 2; n = 1 when m = 1; or n = 0 when m = 2; R4 = R5 = H, or R4R5 = bond when m = 2; R6 = OH, alkoxy]. Also disclosed are preparation of I, compns. containing I, and use of I for treatment of painful, hyperalgesic and/or inflammatory conditions in which C-fibers play a pathophysiol. role by eliciting neurogenic pain or inflammation. For example, 10,11-dihydro-5H-dibenz[b,f]azepine was alkylated in the 5-position by NaH and 3-bromopropyl tetrahydro-2-pyranyl ether, followed by deprotection with HCl in refluxing aqueous MeOH, to give the 5-(3-hydroxypropyl) derivative. This underwent mesylation with MeSO2Cl and Et3N, and the mesylate was treated with (R)-3-piperidinecarboxylic acid Et ester (tartrate salt) and then hydrolyzed to give title compound II, isolated as the HCl salt (III). In the formalin-induced pain response test in mice, III at 0.1 mg/kg gave 50% inhibition.

MSTR 2



G3 = 24-4 25-23 24-9

$2\text{G}^4\text{---}2\text{CH}_2$

G4 = N

G5 = O

G7 = (1-3) CH2

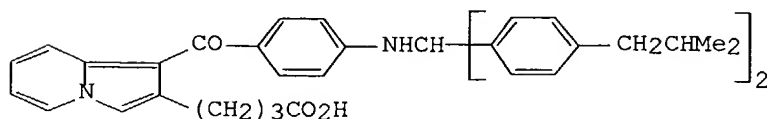
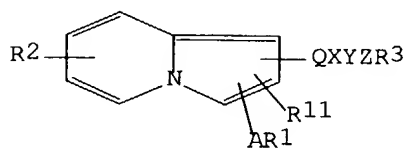
G8 = OSO2C6H4Me-p

MPL: claim 3

L10 ANSWER 10 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
 AN 118:212886 MARPAT Full-text
 TI Preparation of indolizine derivatives as testosterone 5 α -reductase inhibitors
 IN Okada, Satoshi; Sawada, Kozo; Kuroda, Akio; Watanabe, Shinya; Tanaka, Hirokazu
 PA Fujisawa Pharmaceutical Co., Ltd., Japan
 SO Eur. Pat. Appl., 64 pp.
 CODEN: EPXXDW
 DT Patent
 LA English
 FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 519353	A2	19921223	EP 1992-109968	19920613
	EP 519353	A3	19930414		
	EP 519353	B1	20000816		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
	ZA 9203958	A	19930224	ZA 1992-3958	19920529
	US 5334716	A	19940802	US 1992-892453	19920602
	AT 195521	E	20000915	AT 1992-109968	19920613
	ES 2149160	T3	20001101	ES 1992-109968	19920613
	PT 519353	T	20001229	PT 1992-109968	19920613
	HU 61544	A2	19930128	HU 1992-1993	19920615
	CA 2071375	AA	19921218	CA 1992-2071375	19920616
	CA 2071375	C	20030211		
	AU 9218270	A1	19921224	AU 1992-18270	19920616
	AU 656197	B2	19950127		
	CN 1067893	A	19930113	CN 1992-104790	19920616
	CN 1042226	B	19990224		
	JP 05178856	A2	19930720	JP 1992-157074	19920616
	RU 2120942	C1	19981027	RU 1992-5011971	19920616
	GR 3034429	T3	20001229	GR 2000-402118	20000918
PRAI	GB 1991-13027		19910617		
	GB 1991-20764		19910930		
	GB 1991-24345		19911115		
	GB 1992-3809		19920221		

GI



AB Title compds. I [R1 = HO2C, protected-HO2C; R2 = H, alkyl, halo; R3 = (substituted) aryl, aralkyl, -carbamoylethyl, N-heterocyclyl, etc.; R11 = H, alkyl, A = (substituted) alkylene, alkenylene; Q = CO, alkylene; X = (substituted) Ph, furandiyl; Y = bond, alkylene; Z = alkylene, alkenylene, O, R6N wherein R6 = H, (substituted) alkyl, -aralkyl, protecting group] and their salts are prepared To Et 4-[1-(4-aminobenzoyl)indolizin-3-yl]butyrate (preparation given) in CH2Cl2 were added diisopropylethylamine and bis(4-isobutylphenyl)chloromethane in CH2Cl2 to give Et 4-[1-[4-[bis(4-isobutylphenyl)methylamino]benzoyl]indolizin-3-yl]butyrate to which was added 4N NaOH to give title compound II. II showed IC50 of 4.4 + 10-10 M against testosterone 5 α -reductase.

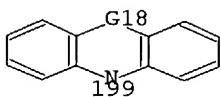
MSTR 3

G16-G17

G16 = OSO2C6H4Me-p
G17 = 224

^{G(O)}₂₂₄-G19

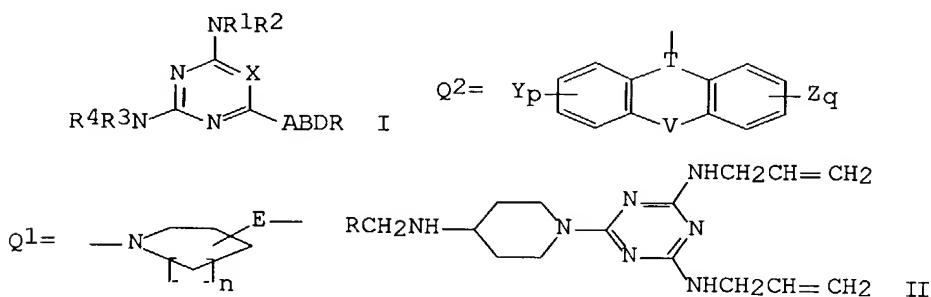
G18 = O
G19 = 199



DER: or salts
MPL: claim 11

L10 ANSWER 11 OF 11 MARPAT COPYRIGHT 2004 ACS on STN
 AN 118:6998 MARPAT Full-text
 TI Preparation of triaminotriazines and analogs as antitumor and antiparasitic adjuncts
 IN Regnier, Gilbert; Dhainaut, Alain; Atassi, Ghanem; Pierre, Alain; Leonce, Stephane
 PA Adir et Cie., Fr.
 SO Eur. Pat. Appl., 36 pp.
 CODEN: EPXXDW
 DT Patent
 LA French
 FAN.CNT 1

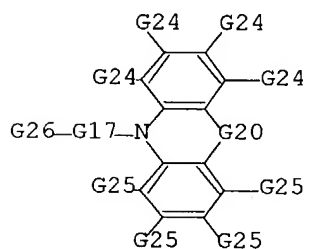
	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 502788	A1	19920909	EP 1992-400578	19920306
	EP 502788	B1	19940511		
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE				
	FR 2673627	A1	19920911	FR 1991-2710	19910307
	FR 2673627	B1	19930507		
	CA 2062378	AA	19920908	CA 1992-2062378	19920306
	AU 9211468	A1	19920910	AU 1992-11468	19920306
	AU 643880	B2	19931125		
	ZA 9201702	A	19921125	ZA 1992-1702	19920306
	JP 05125062	A2	19930521	JP 1992-98998	19920306
	JP 07076216	B4	19950816		
	US 5238936	A	19930824	US 1992-847916	19920306
	AT 105553	E	19940515	AT 1992-400578	19920306
	ES 2056692	T3	19941001	ES 1992-400578	19920306
PRAI	FR 1991-2710		19910307		
	EP 1992-400578		19920306		
GI					



AB Title compds. [I; A = bond, hydrocarbylenediyl, hydrocarbylimino; B = Q'; D = bond, hydrocarbylenediyl; E = O, S, NH, etc.; R = dibenzocyclyl group Q₂; R¹-R⁴ = H, (cyclo)alkyl, alkenyl, haloalkyl, etc.; T = CH, NH, CHCH₂, etc.; V = bond, (CH₂)₁₋₃, CH:CH, CO, CH₂NMe, etc.; Y, Z = H, halo, CF₃, alkyl, alkoxy; n = 1-3; p, q = 1, 2] were prepared. Thus, R⁵CH₂NH₂ (R⁵ = Q₂, T = CH, V = CH₂CH₂) (Q₃) was reductively condensed with 1-[4,6-bis(allylamino)]-4-piperidinone to give title compound II (R

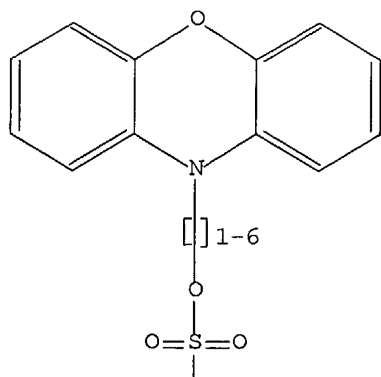
= Q3) which increased survival time of vincristine-resistant leukemia P388-inoculated mice 108% over controls at 50 mg/kg as an adjunct to vincristine.

MSTR 3D



G17 = Ak<(-6)>
G20 = O
G26 = OSO₂C₆H₄Me-p
MPL: claim 10

=> d l1; d his; log y
 L1 HAS NO ANSWERS
 L1 STR



Structure attributes must be viewed using STN Express query preparation.

(FILE 'STNGUIDE' ENTERED AT 11:31:25 ON 20 AUG 2004)
 DEL HIS Y

FILE 'REGISTRY' ENTERED AT 11:31:48 ON 20 AUG 2004
 L1 STRUCTURE UPLOADED
 L2 1 S L1
 L3 3 S L1 FUL

FILE 'CAPLUS' ENTERED AT 11:32:09 ON 20 AUG 2004
 L4 3 S L3

FILE 'BEILSTEIN' ENTERED AT 11:32:48 ON 20 AUG 2004
 L5 0 S L1
 L6 4 S L1 FUL
 L7 1 S L6 NOT L4

FILE 'MARPAT' ENTERED AT 11:33:35 ON 20 AUG 2004
 L8 0 S L1
 L9 12 S L1 FUL
 L10 11 S L9/COM

COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	158.79	512.37
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-7.26	-9.36

STN INTERNATIONAL LOGOFF AT 11:34:39 ON 20 AUG 2004